

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
13 January 2005 (13.01.2005)

PCT

(10) International Publication Number
WO 2005/002576 A2

(51) International Patent Classification⁷: **A61K 31/4184**,
C07D 403/04, A61P 35/00, 31/10

(21) International Application Number:
PCT/GB2004/002913

(22) International Filing Date: 5 July 2004 (05.07.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0315657.7 3 July 2003 (03.07.2003) GB
60/484,685 3 July 2003 (03.07.2003) US
60/514,170 24 October 2003 (24.10.2003) US

(71) Applicant (for all designated States except US): **ASTEX TECHNOLOGY LIMITED** [GB/GB]; 436 Cambridge Science Park, Milton Road, Cambridge CB4 0QA (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BERDINI, Valerio** [GB/GB]; 436 Cambridge Science Park, Milton Road, Cambridge CB4 0QA (GB). **WOODHEAD, Andrew**,

James [GB/GB]; 436 Cambridge Science Park, Milton Road, Cambridge CB4 0QA (GB). **WYATT, Paul, Graham** [GB/GB]; 436 Cambridge Science Park, Milton Road, Cambridge CB4 0QA (GB). **O'BRIEN, Michael, Alistair** [GB/GB]; 436 Cambridge Science Park, Milton Road, Cambridge CB4 0QA (GB). **NAVARRO, Eva, Figueroa** [ES/GB]; 436 Cambridge Science Park, Milton Road, Cambridge CB4 0QA (GB).

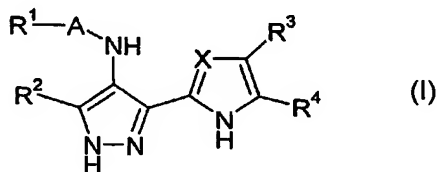
(74) Agent: **HUTCHINS, Michael, Richard**; M.R. Hutchins & Co., 23 Mount Sion, Tunbridge Wells, Kent TN1 1TZ (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH,

[Continued on next page]

(54) Title: PHARMACEUTICAL COMPOUNDS



(57) Abstract: The invention provides a compound of the formula (I): or a salt, N-oxide or solvate thereof; wherein X is CR⁵ or N; A is a bond or -(CH₂)_m-(B)_n; B is C=O, NR⁸(C=O) or O(C=O) wherein R⁸ is hydrogen or C₁₋₄ hydrocarbyl optionally substituted by hydroxy or C₁₋₄ alkoxy; m is 0, 1 or 2; n is 0 or 1; R¹ is hydrogen, a carbocyclic or heterocyclic group having from 3 to 12 ring members, or an optionally substituted C₁₋₈ hydrocarbyl group; R² is hydrogen, halogen, methoxy, or a C₁₋₄ hydrocarbyl group optionally substituted by halogen, hydroxyl or methoxy; R³ and R⁴ are the same or different and each is selected from hydrogen, CN, C(O)R⁸, optionally substituted C₁₋₈ hydrocarbyl and carbocyclic or heterocyclic groups having from 3 to 12 ring members; and R⁵ is hydrogen, a group R² or a group R¹⁰ wherein R¹⁰ is selected from halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino, mono- or di-C₁₋₄ hydrocarbyl amino, carbocyclic and heterocyclic groups having from 3 to 12 ring members; a group R^a-R^b wherein R^a is a bond, 0, CO, X¹C(X²), C(X²)X¹, X¹C(X²)X¹, S, SO, SO₂, NR^c, SO₂NR^c or NR^cSO₂; and R^b is selected from hydrogen, carbocyclic and heterocyclic groups having from 3 to 12 ring members, and a C₁₋₈ hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di-C₁₋₄ hydrocarbylamino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the C₁₋₈ hydrocarbyl group may optionally be replaced by O, S, SO, SO₂, NR^c, X¹C(X²), C(X²)X¹ or X¹C(X²)X¹; R^c is selected from hydrogen and C₁₋₄ hydrocarbyl; X¹ is O, S or NR^c and X² is =O, =S or =NR^c; and R⁸ is selected from OR¹¹, SR¹¹ and NR¹²R¹³; R¹¹ is selected from optionally substituted C₁₋₈ hydrocarbyl and carbocyclic or heterocyclic groups having from 3 to 12 ring members; and one of R¹² and R¹³ is a group R¹¹ and the other of R¹² and R¹³ is hydrogen or C₁₋₄ alkyl; or R¹² and R¹³ and the nitrogen atom to which they are attached together form a saturated heterocyclic group having from 4 to 7 ring members and containing 1,2 or 3 heteroatom ring members selected from N, O and S. The compounds have activity against cyclin dependent kinases glycogen synthase kinase and Aurora kinases.



GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.